

Atty Dkt. No.: 10990105-5
USSN: 09/302,898

AMENDMENTS

Please incorporate the amendments below into the above-referenced application. For convenience, a complete listing of the claims in their current form is provided below.

In the Claims:

1. **(Currently Amended)** A method of fabricating an array of polynucleotides on a substrate, comprising:
 - (a) operating a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate **in accordance with a target array pattern determined by a processor in communication with the deposition system to provide, when dry, a target pattern of polynucleotide-containing spots;**
 - (b) allowing a sufficient time to pass such that droplets deposited by the system will have dried to yield an actual pattern of dried spots; and
 - (c) observing the actual pattern; and
 - (d) comparing the actual pattern with the target pattern **of polynucleotide containing spots.**
2. **(Original)** A method according to claim 1 wherein the actual pattern is observed by capturing an image of the actual pattern.
3. **(Original)** A method according to claim 1 wherein the system deposits fluid droplets at least some of which contain respective different polynucleotides.
4. **(Original)** A method according to claim 1 wherein the one or more polynucleotide containing fluids each comprise a solution of a polynucleotide and a sufficient amount of salt to enhance polynucleotide imaging.
5. **(Original)** A method according to claim 1 wherein the polynucleotides are DNA of at least six nucleotides in length.
6. **(Original)** A method according to claim 5 wherein the DNA is cDNA.

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7. (Original) A method according to claim 5 wherein the DNA is single stranded.
8. (Original) A method according to claim 1 wherein the comparison includes a comparison of dried actual spot locations or dimensions with target locations or dimensions.
9. (Original) A method according to claim 1 wherein the comparison includes a comparison of the presence or absence of dried spots at target locations.
10. (Original) A method according to claim 1 wherein the image capture comprises imaging a light scattering characteristic of dried spots.
11. (Original) A method according to claim 1 wherein the image capture comprises imaging a fluorescence characteristic of dried spots.
12. (Original) A method according to claim 1 additionally comprising generating a signal indicative of the result of the comparison.
13. (Original) A method according to claim 1 wherein the deposition system is operated to fabricate multiple polynucleotide arrays on a same substrate.
14. (Original) A method according to claim 1 additionally comprising:
when the results of one or more comparisons for an array exceed a predetermined tolerance, storing an error indication in association with that array.
15. (Original) A method according to claim 14 wherein the deposition system is operated to fabricate multiple polynucleotide arrays, the method additionally comprising rejecting the array associated with a stored error indication.
16. (Original) A method according to claim 14 wherein the error indication is stored in a memory, the method additionally comprising writing on a medium an identification for the array associated with an error indication; physically associating that medium with the array; and storing the identification in the memory.

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17. (Original) A method according to claim 16 wherein the error indication includes an indication of the magnitude of the error.

18. (Currently Amended) A method of fabricating an array of polynucleotides on a substrate, comprising:

(a) operating a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system to provide a target pattern of polynucleotide-containing spots which may differ from the actual pattern deposited;

(b) capturing an image of the actual pattern;

(c) comparing the actual pattern with the target pattern ~~of polynucleotide containing spots~~;

(d) when the results of one or more comparisons for an array identify the presence of a first level error, generating a first level error indication associated with the array;

(e) writing the error indication or an identification of the error indication, on a medium; physically associating the medium with the array; and, when an identification of the error indication is written on the medium, storing the identification in a memory in association with the error indication; and

(f) forwarding the array and medium to a remote user.

19. (Canceled)

20. (Original) A method according to claim 1 wherein the polynucleotide deposition system automatically fabricates multiple polynucleotide arrays, the method additionally comprising, when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, automatically halting further operation of the deposition system and generating a visible or audible operator alert.

21. (Original) A method according to claim 1 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, the method additionally comprising:

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when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication;

when multiple error conditions are generated, evaluating if a same drop dispenser is responsible;

and wherein, when the evaluation indicates the same drop dispenser is responsible, generating a visible or audible operator alert which includes an indication of the responsible drop dispenser.

22. (Original) A method according to claim 21 wherein the indication of the responsible drop dispenser comprises an indication of potential error in a polynucleotide containing fluid which has been preselected to be dispensed by that drop dispenser.

23. (Original) A method according to claim 1 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, the method additionally comprising:

the control processor loading the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid;

when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication;

when multiple error indications are generated, the control processor comparing a pattern of error indications with the loading pattern of the dispensers to evaluate whether one or more drop dispensers or an error in a polynucleotide containing fluid is responsible for the error indications.

24. (Original) A method according to claim 13 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and each array is to be deposited using an initial pattern of drop dispensing from the multiple dispensers, the method additionally comprising:

when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication;

when multiple error indications are generated, evaluating if a same drop dispenser may be responsible; and

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when the evaluation indicates the same drop dispenser may be responsible, altering the initial pattern such that the same drop dispenser is not used.

25. **(Currently Amended)** An apparatus for fabricating an array of polynucleotides on a substrate, comprising:

(a) a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system to provide, when dry, a target pattern of polynucleotide containing spots;

(b) an imaging system to capture an image of an actual pattern of dried spots resulting from drying of droplets deposited on the substrate;

(c) a processor to control the deposition system to deposit the array of droplets and which, after a predetermined time has elapsed for drying of the droplets to yield the actual pattern, causes the imaging system to capture the actual pattern and compares actual pattern with the target pattern ~~of polynucleotide containing spots.~~

26. **(Original)** An apparatus according to claim 25 wherein the deposition system deposits droplets of no greater than 1000 pL.

27. **(Original)** An apparatus according to claim 25 wherein the deposition system includes a head having multiple pulse jets each of which can dispense droplets of a fluid onto a substrate, each jet including a chamber with an orifice, and including an ejector which, when activated, causes a droplet to be ejected from the orifice.

28. **(Original)** An apparatus according to claim 27 wherein the head has at least ten jets.

29. **(Original)** An apparatus according to claim 27 wherein the imaging system captures a light scattering characteristic of dried spots.

30. **(Original)** An apparatus according to claim 27 wherein the imaging system captures a fluorescence characteristic of dried spots.

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31. (Original) An apparatus according to claim 25 wherein the processor automatically: operates the deposition system to deposit multiple polynucleotide arrays; causes the imaging system to capture one or more of the images; and performs the comparison step for such arrays.

32. (Original) An apparatus according to claim 25 additionally comprising a memory, and wherein when the results of one or more comparisons for an array exceed a predetermined tolerance, the processor stores in the memory an error indication in association with an identification of that array.

33. (Original) An apparatus according to claim 32 wherein the error indication includes an indication of the magnitude of the error.

34. (Original) An apparatus according to claim 25 additionally comprising an audio or visual output device, and wherein:

the polynucleotide deposition system automatically fabricates multiple polynucleotide arrays; and

when the results of one or more comparisons for an array exceed a predetermined tolerance indicating an error condition, the processor automatically halts further operation of the deposition system and generates a visible or audible operator alert on the output device.

35. (Original) An apparatus according to claim 25 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, and wherein the processor:

generates an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance; and

when multiple error conditions are generated, evaluates if a same drop dispenser may be responsible

36. (Original) An apparatus according to claim 35 additionally comprising an audio or visual output device, and wherein when the evaluation indicates a same drop dispenser

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may be responsible the processor generates an operator alert on the output device which includes an indication of the responsible drop dispenser.

37. (Previously Presented) An apparatus according to claim 25 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers, the apparatus additionally comprising a memory, and wherein the processor:

- activates the drop dispensers in accordance with an initial pattern stored in the memory;
- generates an error indication when the results of one or more comparisons for an array exceed a predetermined tolerance; and
- evaluates if a same drop dispenser or an error in a polynucleotide containing fluid may be responsible by comparing the stored dispensing pattern with a pattern of error indications.

38. (Original) An apparatus according to claim 37 wherein the processor alters the initial pattern in response to the result of the evaluation of the drop dispenser or polynucleotide containing fluid error.

39. (Currently Amended) An apparatus for fabricating an array of polynucleotides on a substrate, comprising:

- (a) a polynucleotide deposition system to deposit an array of polynucleotide containing fluid droplets on the substrate in accordance with a target array pattern determined by a processor in communication with the deposition system to provide a target pattern of polynucleotide containing spots which may differ from the actual pattern deposited;

- (b) an imaging system to capture an image of the actual pattern of spots;

- (c) a processor to control the deposition system to deposit the array of droplets and which causes the imaging system to capture the actual pattern and compares the actual pattern with the target pattern ~~of polynucleotide containing spots~~;

wherein:

- the deposition system includes a head retainer to receive a fluid dispensing head, and includes a transporter to move the head retainer relative to the substrate;

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the imaging system includes a light receiving element mounted for movement by the transporter.

40. (Original) An apparatus according to claim 39 wherein the light receiving element includes a light sensor.

41. (Previously Presented) A method according to claim 1 wherein the actual pattern is compared with the target pattern for spot location, dimension or presence, the method additionally comprising generating a signal indicative of the result of the comparison.

42. (Previously Presented) An apparatus according to claim 25 wherein the processor compares the actual pattern with the target pattern for spot location, dimension or presence, and additionally generates a signal indicative of the result of the comparison.

43. (Previously Presented) A method according to claim 1 wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, the method additionally comprising the control processor:

loading the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid;

performing the comparisons of the actual and target patterns and, when the results of one or more comparisons for an array exceed a predetermined tolerance, generating an error indication; and

when an error indication is generated, operating the drop dispensers to correct for the error.

44. (Previously Presented) A method according to claim 43 wherein when the error indication is caused by incorrect drop dispenser operation, the processor uses another drop dispenser to correctly deposit a drop on the same array.

45. (Previously Presented) A method according to claim 44 wherein the drop dispensers are pulse jets.

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46. (Previously Presented) An apparatus wherein the polynucleotide deposition system includes a fluid dispensing head with multiple drop dispensers and a control processor, wherein the control processor:

loads the dispensers in a pattern in which at least some of the dispensers are loaded with the same fluid;

performs the comparisons of the actual and target patterns and, when the results of one or more comparisons for an array exceed a predetermined tolerance, generates an error indication; and

when an error indication is generated, operating the drop dispensers to correct for the error.

47. (Previously Presented) An apparatus according to claim 46 wherein when the error indication is caused by incorrect drop dispenser operation, the processor uses another drop dispenser to correctly deposit a drop on the same array.

48. (Currently Amended) An apparatus method according to claim 47 wherein the drop dispensers are pulse jets.